# **HPV Vaccine Information for Clinicians**

CDC recommends HPV vaccination for girls and boys at ages 11 or 12 years to protect against cancers caused by HPV infections. CDC encourages clinicians to recommend HPV vaccination the same way and same day they recommend other routinely recommended vaccines for adolescents.

### **Background**

Human papillomavirus (HPV) is a very common virus that infects epithelial tissue. More than 120 HPV types have been identified. Most HPV types infect cutaneous epithelial cells and cause common warts, such as those that occur on the hands and feet. Approximately 40 HPV types infect mucosal epithelial cells on the genitals, and the mouth and throat. Although most HPV infections are asymptomatic and resolve spontaneously or become undetectable, some HPV infections can persist and lead to cancer.

Persistent infections with high-risk (oncogenic) HPV types can cause cancers of the anus, cervix, penis, vulva, and vagina, as well as the oropharynx (defined as the back of the throat, including the base of the tongue and tonsils). The most common high-risk types are 16 and 18.

Infection with low-risk (non-oncogenic) HPV types can cause genital warts and rarely laryngeal papillomas. These types can also cause benign or low-grade cervical cell abnormalities. The most common low-risk HPV types are 6 and 11.

About 79 million Americans are infected with HPV, and roughly 14 million people become infected each year, mostly occurring among teens and young adults. Almost every person who is sexually active will acquire HPV at some time in their life.

Every year in the United States, an estimated 17,600 women and 9,300 men are diagnosed with a cancer caused by HPV.

Of the women diagnosed with an HPV cancer, cervical cancer is the most common with about 11,000 women diagnosed annually in the United States; subsequently about 4,400 women die every year from cervical cancer in our country.

Of the men in the United States diagnosed with an HPV cancer, oropharyngeal cancer is the most common. Around 7,200 U.S. men each year are diagnosed with oropharyngeal cancer caused by HPV infection. HPV infection and precancerous/dysplastic lesions of the oropharynx cannot be screened for, making prevention of infection a priority.

### **HPV Vaccines**

Three HPV vaccines have been licensed by the U.S. Food and Drug Administration (FDA) since 2006. CDC recommends these HPV vaccines for routine use among girls and boys at ages 11 or 12. HPV vaccines are administered as a 3-dose series with doses given at 0, 1-2, and 6 months.

	Bivalent/2vHPV (Cervarix)	Quadrivalent/4vHPV (Gardasil)	9-valent/9vHPV (Gardasil 9)
Manufacturer	GlaxoSmithKline	Merck	Merck
Year Licensed	October 2009 - females	June 2006 - females; October 2009 - males	December 2014 - males and females
HPV types in vaccine	16 and 18	6, 11, 16, and 18	6, 11, 16, 18, 31, 33, 45, 52, and 58
Adjuvant in vaccine	ASO4: 500 μg aluminum hydroxide 50 μg 3- <i>O</i> -desacyl-4′-monophosphoryl lipid A	AAHS: 225 µg amorphous aluminum hydroxyphosphate sulfate	AAHS: 500 µg amorphous aluminum hydroxyphosphate sulfate
Recommended for	Females ages 11-12     Females ages 13 through 26 who have not been previously vaccinated	Females and males ages 11-12 Females ages 13 through 26 and males ages 13 through 21 who have not been previously vaccinated Unvaccinated males ages 22 through 26 who have sex with men or who are immunocompromised	Females and males ages 11-12     Females ages 13 through 26 and males ages 13 through 21 who have not been previously vaccinated     Unvaccinated males ages 22 through 26 who have sex with men or who are immunocompromised
Contraindicated for	People with hypersensitivity to latex	People with hypersensitivity to yeast	People with hypersensitivity to yeast



Bivalent, quadrivalent, and 9-valent HPV vaccine all protect against HPV 16 and 18, the HPV types that cause about 66% of cervical cancers and the majority of other HPV-attributable cancers in the United States. 9-valent HPV vaccine targets five additional cancer-causing types, which account for about 15% of cervical cancers (12). Quadrivalent and 9-valent HPV vaccine also protect against HPV 6 and 11, the HPV types that cause anogenital warts.

The additional five types in 9-valent HPV vaccine account for a higher proportion of HPV-associated cancers in women compared with men, and also cause cervical precancers in women. Therefore, the additional protection from 9-valent HPV vaccine will mostly benefit women.

## **HPV Vaccine Recommendations**

HPV vaccine is routinely recommended for 11- or 12-year-old girls and boys. Any HPV vaccine can be given to girls. Either the quadrivalent or 9-valent HPV vaccine can be given to boys. Vaccination is also recommended for females ages 13 through 26 years and males ages 13 through 21 years who were not vaccinated when they were younger. Vaccination is also recommended for both men who have sex with men and men who are immunocompromised (including men with HIV infection) aged 22 through 26 years who were not vaccinated when they were younger.

Ideally, patients should be vaccinated before they are exposed to HPV. However, patients who have already been infected with one or more HPV types can still get protection from other HPV types in the vaccine that have not been acquired.

#### HPV vaccines can safely be given to...

- Patients with minor acute illnesses, such as diarrhea or mild upper respiratory tract infections, with or without fever.
- Women who have had an unclear or abnormal Pap test, a positive HPV test, or genital warts. However, these patients should be advised that the vaccine may not have any therapeutic effect on existing Pap test abnormalities, HPV infection, or genital warts.
- Patients who are immunocompromised, either from disease or medication. However, the immune response to vaccination and effectiveness of the vaccine might be less than in people with a normally functioning immune system.
- Women who are breastfeeding.

#### HPV vaccines should not be given to...

- Patients with a history of allergies to any vaccine component. Quadrivalent vaccine (4vHPV) is not recommended for people with a history of allergies to yeast. Bivalent vaccine (2vHPV) is not recommended for people with a life-threatening latex allergy.
- Patients with moderate or severe acute illnesses. In these cases, patients should wait until the illness improves before getting vaccinated.
- Pregnant women. However, the vaccine has not been linked to causing adverse pregnancy outcomes or possible side effects (adverse events) to the developing fetus.
  - If a woman is found to be pregnant after starting the HPV vaccine series, second and/ or third doses should not be given until after delivery.
  - If a woman receives HPV vaccine and later learns that she is pregnant, there is no reason to be alarmed.
  - 9vHPV exposure during pregnancy <u>should</u> be reported to the Merck Pregnancy Registry at 1-800-986-8999.
  - 4vHPV exposure during pregnancy can be reported to Merck at 1-877-888-4231.
  - 2vHPV exposure during pregnancy <u>can</u> be reported to GlaxoSmithKline at telephone 1-888-825-5249.
  - 2vHPV exposure during pregnancy <u>can</u> be reported to GlaxoSmithKline at telephone 1-888-825-5249.

## **HPV Vaccine Safety**

HPV vaccines are very safe. Scientific research shows the benefits of HPV vaccination far outweigh the potential risks. Like all medical interventions, vaccines can have some side effects. More than 80 million doses of HPV vaccine have been distributed since the vaccine was introduced in 2006. The most common side effects associated with HPV vaccines are mild, and include pain, redness, or swelling in the arm where the shot was given.

All vaccines used in the United States, including HPV vaccines, are required to go through years of extensive safety testing before they are licensed by the U.S. Food and Drug Administration (FDA). During clinical trials conducted before they were licensed:

- 9-valent HPV vaccine was studied in more than 15,000 males and females
- Quadrivalent HPV vaccine was studied in more than 29,000 males and females
- Bivalent HPV vaccine was studied in more than 30.000 females

Each HPV vaccine was found to be safe and effective.

Fainting (syncope) can occur after any medical procedure, including vaccination. Recent data suggest that syncope after any vaccination is more common in adolescents. Adolescents and adults should be seated or lying down during vaccination. Providers are encouraged to observe patients in seated or lying positions for 15 minutes after vaccination. This is to prevent any injuries that could occur from a fall during a syncopal event.

#### **HPV Vaccine Effectiveness**

The HPV vaccine works extremely well. In the four years after the vaccine was recommended in 2006 in the United States, quadrivalent type HPV infections in teen girls decreased by 56% and decreases in prevalence have also been observed in women in their early 20s. Research has also shown that fewer teens are getting genital warts since HPV vaccines have been in use in the United States. Decreases in vaccine-type prevalence, genital warts, and cervical dysplasia have also been observed in other countries with HPV vaccination programs.

There are no data to suggest HPV vaccines will treat existing diseases or conditions caused by HPV. However, people can still get protection from HPV types in the vaccine that have not been acquired.

Cervical cancer screening is recommended for women beginning at age 21 years and continuing through age 65 years. Women who have received the HPV vaccine series should still be screened for cervical cancer beginning at age 21 years, in accordance with currently published cervical cancer screening guidelines.

## **Duration of Vaccine Protection**

Studies suggest that HPV vaccines offer long-lasting protection against HPV infection and therefore disease caused by HPV infection. Studies of the bivalent and quadrivalent vaccines have followed vaccinated individuals for eight to ten years and have found no evidence of protection decreasing over time. Duration of protection provided by HPV vaccination will continue to be studied.

### **HPV Vaccine Administration**

HPV vaccines should be administered as a 3-dose series intramuscular injections given at 0, 1-2, and 6 months. The third dose should follow the first dose by at least 24 weeks.

While there is a minimum interval in the dosing schedule, there is no maximum interval. There is no reason to restart the vaccine series if the HPV vaccine schedule is interrupted; patients who have exceeded the minimum interval for the next dose by months or even years, may be given the next dose needed.

Vaccination of females is recommended with bivalent, quadrivalent (as long as this formulation is available), or 9-valent HPV vaccine. Vaccination of males is recommended with quadrivalent (as long as this formulation is available) or 9-valent HPV vaccine.

If vaccination providers do not know or do not have available the HPV vaccine product previously administered, or are in settings transitioning to 9-valent HPV vaccine, any available HPV vaccine product may be used to continue or complete the series for females for protection against HPV 16 and 18; 9vHPV or 4vHPV may be used to continue or complete the series for males. There are no data on efficacy or immunogenicity of fewer than 3 doses of 9vHPV.

HPV vaccine can safely be administered at the same visit as other vaccines recommended at ages 11 or 12 years, such as Tdap vaccine, quadrivalent meningococcal conjugate vaccine, and influenza vaccine. Administering all indicated vaccines at a single visit at ages 11 or 12 years increases the likelihood that patients receive their vaccinations on schedule.

As mentioned previously, patients should be observed for 15 minutes after receiving any shot, including HPV vaccine.

## **Paying for HPV Vaccine**

As with all vaccines recommended by the Advisory Committee on Immunization Practices (ACIP), HPV vaccines are covered by insurance. For patients that need assistance paying for HPV vaccine, the Vaccines for Children (VFC) program may be able to help. VFC provides vaccines for children ages 18 years and younger who are uninsured, Medicaid-eligible, or American Indian/Alaska Native. Learn more about the VFC program at <a href="https://www.cdc.gov/Features/VFCprogram/">www.cdc.gov/Features/VFCprogram/</a>.

### **Related Resources**

Epidemiology and Prevention of Vaccine-Preventable Diseases (Pink Book) 2015.

Markowitz L, Dunne EF, Saraiya M, Curtis RC, Gee J, Bocchini JA, et al. <u>Human papillomavirus vaccination: recommendations of the Advisory Committee on Immunization Practices (ACIP)</u>. MMWR. 2014 Aug 29; 63(rr05):1-30.